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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/523,102	03/10/2000	Erwin Si	03654.0255	4492

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EXAMINER	
SAUCIER, SANDRA E	

ART UNIT	PAPER NUMBER
1651	19

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/523,102	SI ET AL.	
	Examin r	Art Unit	
	Sandra Saucier	1651	

-- *The MAILING DATE of this communication appears on the c ver sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *43-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 March 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/26/03, 9/24/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-66 are pending. Claims 1-42 are considered on the merits. Claims 43-66 are withdrawn from consideration as being drawn to a non-elected invention.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112
INDEFINITE

Claims 1, 2, 4-8, 10-16, 18-24, 26-34, 36-39, 41 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite using "a batimastat compound". However, no definition of what constitutes "a batimastat compound" is found in the claim or the body of the specification. For example, how closely related does a compound have to be to fall within the limitation of "a batimastat compound". Do salts and esters fall within this limitation? Would a compound which lacks the terminal methyl on the amine group be considered to fall within or outside of the phrase "a batimastat compound"? Would the related compound, marimastat be considered to be "a batimastat compound"? Please point to a definition in the specification of what comprises a batimastat compound as used in the claims.

Response to Arguments

Applicant's arguments filed 8/26/03 have been fully considered but they are not persuasive.

Applicants argue that one of skill in the art would know what a "batimastat compound" is. However, no objective evidence is offered to delineate the metes and bounds of this term and the claim language is not limited by the disclosure of the specification.

This argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Counsel's arguments cannot take the place of objective evidence.

While the claims are read in light of the specification, limitations appearing in the specification are not read into the claim.

Claim Rejections - 35 USC § 103

Claims 1-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,767,153 [A] and WO 97/41844 [AH1] or US 5,763,621 [AC2].

The claims are directed to a method of treating retinal neovascularization in an animal comprising topically administering a composition comprising 0.01-3% w/w batimastat and a polymeric suspension agent, particularly polycarbophil.

The references are relied upon as explained below.

US 5,767,153 discloses a composition comprising 0.3% batimastat and 1.15% polycarbophil useful for topical ophthalmic administration, example 7. It teaches that

inclusion of medicaments such as batimastat in combination with polycarbophil increases its bioavaliability to the target tissue in the eye.
The reference lacks the disclosure of use of the composition of polycarbophil and batimastat for the treatment of retinal neovascularization.

WO 97/41844 discloses that batimastat is an angiostatic agent and as such is effective in compositions for the treatment of diseases where neovascularization arises such as diabetic retinopathies, proliferative virtreoretinopathies and other diseases (page 1, second paragraph and page 5, table 1). Compositions comprising metalloproteinase inhibitors such as batimastat, which is a preferred angiostatic agent (page 19, l. 9) are in topical ophthalmic formulations (claim 20). The compositions may be used to prevent retinal neovascularization (page 20, l. 11).

US 5,763,621 discloses that metalloproteinase inhibitors are useful in the prophylaxis or treatment of proliferative retinopathies. Batimastat (BB-94) is taught to belong to the class of hydroxamic acid metalloproteinase inhibitors (col. 1, ls. 20-30 and col. 2, l. 35).

The substitution of the composition of batimastat and polycarbophil disclosed in US 5,767,153 for the batimastat composition taught in the methods of WO 97/41844 or US 5,763,621 would have been obvious because batimastat is known to be useful to treat retinal neovascularization as taught in '844 or '621 and the formulation of batimastat with polycarbophil as a suspension agent is taught in '153 to be particularly advantageous in terms of delivering a sustained dosage of a sparingly water soluble active ingredient such as batimastat over time.

One of ordinary skill in the art would have been motivated at the time of invention to substitute a composition of batimastat for a composition of batimastat and polycarbophil to treat retinal neovascularization in order to obtain the results as suggested by the references with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

Response to Arguments

Applicants argue that there is no suggestion to substitute the batimastat composition of '153 in the methods of '844 or '621 and that the examiner used hindsight.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants argue that the examiner has applied an "obvious to try" standard. However, since motivation to substitute the composition of example 7, for instance, for the compositions in the methods taught in the secondary references is found in the primary reference of '153 where it is stated that the inclusion of a medicament in an emulsion with a lightly crosslinked polymer (polycarbophil) (col. 4, l. 1-15), abstract, for administration to the eye promotes the medicaments' bioavailability (col. 5, l. 19-35). Specifically

exemplified is batimastat and polycarbophil. Such a combination is directly taught by the reference to be superior to administration of batimastat alone in terms of sustained release and bioavailability. This appears to be a high level of motivational direction.

Applicants argue that the administration of this composition would not reasonably be expected to accomplish therapeutic delivery to the retina.

First, the claims do not specify that the composition is delivered to the retina.

Second, even if they did, it might be an inherent effect of the one step method of administering to the eye.

Third, the secondary reference of '844 teaches that diabetic retinopathies and proliferative vireoretinopathies (page 1) involve angiogenesis, presumably in the retina. Since the method of '844 includes a topical administration (page 23, line 1), it is assumed that the inference is that the medicament is expected to reach the retina in the absence of evidence to the contrary. The secondary reference of '621 teaches topical application to the eye of batimastat (col. 11, l. 46) for treatment of proliferative retinopathies (col. 1, l. 30). Thus, both references generically teach topical administration for treatment of proliferative retinopathies.

Applicants argue that '844 teaches away from the topical application of batimastat for treatment of retinal disorders, and that it teaches the topical administration of batimastat for treatment of directly accessible tissues for pytergium, hyperderatosis, cheloid and polyp formation on page 24. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. The reference of '844 does not state that a topical application of batimastat is not effective for treatment of the retina and in fact, teaches in Examples 1 and 2, topical composition useful for controlling ocular neovascularization. The term, "ocular" includes the retina.

Applicant has submitted a reference by Geroski et al. which is published in 2000. Applicants' arguments on page 5, last line of the second paragraph state "see n.J., at 461". This is not a decipherable citation. The examiner has assumed for sake of argument that applicant is referring to Geroski et al.. Although Geroski et al. teaches that topical application of solutions to the eye as drops permits less than 5% of the medicament to reach intraocular tissue, topical formulations remain effective, largely because of the very high concentration of drugs that are administered. See page 961, first column. Thus, the topical administration of drugs to the eye, although, not 100% efficient, is effective to reach intraocular tissue, the retina is an intraocular tissue. Applicants have not demonstrated or pointed out that their dosages are less than dosages disclosed in the prior art. Further, the advantages of the formulation of batimastat and polycarbophil are taught by '153 to be advantageous since they are sustained release emulsions.

Applicants' examples in the specification have been carefully considered. While they appear to demonstrate batimastat delivery to the retina using polymeric compositions, no comparison of the efficacy of drug delivery using the composition of '844 or '153 has been presented. Such direct comparisons might advance prosecution.

Conclusion

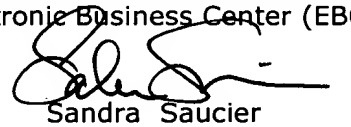
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Saucier whose telephone number is 571-272-0922. The examiner can normally be reached on Monday, Tuesday, Wednesday.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Sandra Saucier
Primary Examiner
Art Unit 1651